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**Sensitivity, specificity and accuracy of the targeted (SRM) and shotgun (panoramic) mass-spectrometry technologies**

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There are about 2,579 missing proteins (NeXtProt PE2,3,4) in the human proteome. They have not been detected in any biological sample using existing experimental methods. They may be not translated, or presented in low-copied state, so existing methods could not be used to detect them. In this work, we compared existing proteomic mass spectromic technologies by using UPS2 set as control (Sigma-Aldrich) and Chromosome 18 encoded proteins detected in human liver and HepG2 cells. Targeted (Selected reaction monitoring, SRM) and panoramic (Shotgun LC-MS/MS) mass spectrometric methods were compared by sensitivity, specificity and accuracy similarly to the FDA diagnostic methods. Transcriptomic analysis of the same sample of human liver and HepG2 cells, or calibration standard UPS2 set was used as a “golden” standard. Proteomic analysis results were compared with the golden standard for true and false identifications revealing. Mass spectromic methods were evaluated using FDA indicators. Sensitivity of SRM in pure UPS2 solution is 92% (44 proteins from 48 detected) and in biological matrix (*E. coli* extract or human blood plasma) it decreases to 63%. Shotgun LC-MS/MS reveals 23 proteins in the pure UPS2 solution and 11 proteins in *E. coli* extract. In HepG2 cell line and liver tissue shotgun LC-MS/MS demonstrated sensitivity 6% and SRM - 35% with the transcriptome “golden” standard. Both methods have high specificity (more than 90%), but the accuracy is only 57% for SRM and 19% for shotgun. Using indicators of sensitivity, specificity and accuracy for proteomic methods demonstrated, that proteins are “missing” in the sample due to different reasons. For example, chemical noise from other molecules in the biological matrix may interfere signal/noise ratio. As a result, MS-signals from presenting proteins may be lost or new MS-signals may appear that is the reason of false positive results. Thus, biological matrix significantly affects the list of detected proteins, which are existing in the mixture in low-copied state ( $\leq 10^{-9}M$ , 109 copies in 1 $\mu$ L).

**Recent Publications**

- Zgoda V G et al. (2013) Chromosome 18 transcriptome profiling and targeted proteome mapping in depleted plasma, liver tissue and HepG2 cells. *Journal of Proteome Research*. 12(1): 123–134.
- Ponomarenko E A et al. (2014) Chromosome 18 transcriptoproteome of liver tissue and HepG2 cells and targeted proteome mapping in depleted plasma. *Journal of Proteome Research*. 13(1): 183–190.
- Poverennaya E V et al. (2016) State of the art on chromosome 18-centric HPP in 2016: Transcriptome and proteome profiling of liver tissue and HepG2 cells. *Journal of Proteome Research*. 15(11): 4030–4038.

**Biography**

Alexander I Archakov is a Full Member of the RAS, Professor and Scientific Advisor of Institute of Biomedical Chemistry. He had organized a scientific school to study molecular organization and functioning of oxygenase cytochrome P450-containing systems, molecular mechanisms of the structure and function of membranes and biological oxidation. Under his guidance, the institute’s members have developed a fundamentally new pharmaceutical composition “Phosphogliv” with antiviral activity for the treatment of liver diseases of various etiology. His present-day/current areas of expertise relate to research in the field of post-genomic technologies, nanobiotechnologies, proteomics, development of approaches to create personalized medicine of the future. He is the pioneer in the development of proteomics in Russia. Currently, he is the international “Human proteome” Project Coordinator in Russia/the coordinator representing Russia in the international “HP” project. He is one of the Russia’s top 100 scientists by Hirsch number-27. He is the author of more than 700 scientific works including about 482 scientific articles, 6 monographs, 30 patents and author’s certificates. He was Scientific Adviser for 15 Doctor students and more than 60 PhD theses. He is a winner of three State Prizes of the USSR, the RSFSR and of the Russian Federation, the Russian Federation Government Award, the Bach Prize of the USSR Academy, the Order “For Merit to the Fatherland” (IV, III, II class).

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